# 0102

## Atherogenic lipid profile and lipid peroxide products of patients with rheumatoid arthritis

Sonia Hammami* (1), Ines Knani (1), Olfa Berriche (2), Saousen Zrour (3), Hassen Bouzidi (3), Naceur Bergaoui (3), Mohamed Hammami (3), Mohsen Kerkni (3)
*(1) Faculté de Médecine Monastir, Monastir, Tunisie – (2) Hôpital Mahdia, Mahdia, Tunisie – (3) Hôpital F. Bourguiba, Monastir, Tunisie*
*Corresponding author: sonia.hammami@fmm.rnu.tn (Sonia Hammami)

*Introduction* Rheumatoid Arthritis (RA) is a chronic relapsing immune-inflammatory multisystem disease with predominant synovial proliferation and destruction of articular cartilage. Patients with RA have a higher riskof mortality related to increased risk of cardiovascular disease with atherogenic lipid profile. In recent years, oxidative stress in RA patients has received considerable attention and has been implicated as mediators of tissue damage and cardio-vascular disease in patients with RA.

The aim of the present study was to assess the lipid profile and lipid peroxide products of patients with rheumatoid arthritis compared with healthy controls.

*Patients and Methods* The study included 70 patients of rheumatoid arthritis who met the American College of Rheumatology (ACR) criteria were included in the study and were compared to 40 healthy volunteers subjects. Patients suffering from diabetes mellitus, hypothyroidism, liver or kidney disease, Cushing's syndrome, obesity, familiar dyslipidemia and those receiving medications affecting lipid metabolism were excluded from the study. Blood samples of controls and patients were collected at the time of presentation and analyzed for lipid profile (total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol) and triglycerides (TG); malondialdehyde (MDA-marker of oxidative stress) and Conjugated Diene (CD) of RA versus healthy subjects.

*Results* Patients exhibited higher serum levels of TC, LDL-C and TG, whereas their serum HDLC levels were significantly lower compared to controls. As a consequence, the atherogenic ratio of TC/HDL-C (3,67±0,83 vs 4,51±1,12; p<0,001) as well as that of TG/HDL-C (0,71±0,19 vs 2,00±0,37; p<0,001), was significantly higher in RA patients compared to controls. The plasma MDA levels(0,57±0,37 vs 0,8±0,20; p<0,001) , the erythrocyte MDA levels(14,78±2,7 vs 22,54±4,25; p<0.001), as well as the plasma CD (121,65±36,75 vs 141,85±50,8; p<0,05) and the erythrocyte CD (142,23±54,74 vs 224,64±73,21, p<0,001) were higher in the patient group than in the control group.

*Conclusion* According to our results, patients with RA exhibited an atherogenic lipid profile with increased levels of oxidative stress markers. This situation accelerates vascular risk in RA. The results suggest the necessity for therapeutic co-administration of antioxidants along with conventional drugs to such patients. However, due to the limited number of cases included in this study, more studies may be required.

*The author hereby declares no conflict of interest*

# 0126

## New regulators of iron metabolism, Hepcidin and Erythroferrone, in acute myocardial infarction.

Aurélie Gudjoncik (1), Julie Lorin (2), Eve Rigal (2), Séverine Claes (2), Catherine Vergely (2), Marianne Zeller* (2), Yves Cottin (2), Luc Rochette (2)
*(1) CHU Dijon, Bocage, Dijon, France – (2) Université de Bourgogne, INSERM U866, Dijon, France*
*Corresponding author: marianne.zeller@u-bourgogne.fr (Marianne Zeller)

*Background* Dysfunctional iron storage and transport are common in patients with chronic heart failure and associated with poor prognosis. Body iron could contribute to the pathogenesis of coronary artery disease (CAD) through its ability to induce oxidative stress. However, studies on the relationship between iron metabolism and CAD have yielded conflicting results.

*Patients and Methods* From the obseRvatoire des Infarctus de Côte d'Or (RICO) survey, 31 consecutive patients admitted in Intensive Care Unit for a first AMI were included. Serum concentrations of iron, transferrin, ferritin, the iron-regulatory hormone hepcidin and erythroferrone (a new hepcidin-regulating hormone), transferrin saturation and total iron binding capacity were assessed on admission.

*Results* Mean age was 65±16 yrs, 61% were male, 51% had hypertension, 23% diabetes, 45% dyslipidemia and 32% were smokers. There was a trend toward a higher serum hepcidin concentration in men (99.8 versus 56.3 ng/ml, p=0.181). Heart rate on admission was negatively associated with an erythroferrone concentration (r=–0.428, p=0.023).

Haemoglobin level and hematocrit were positively correlated with erythroferrone concentration (p=0.027 and p=0.021).

Moreover, a lower serum transferrin concentration was found in patients with heart failure on admission (1.93±0.16g/l, vs 2.32±0.42, p=0.001).

Ferritin concentration was positively related with infarct size, as assessed by Creatine Kinase peak (r=0.535, p=0.002) and there was a trend toward a positive correlation with erythroferrone concentration (r=0.314, p=0.085).

*Conclusion* Elucidating the metabolic circuits regulated by peptidic hormones will provide valuable insights into complex networks governing iron availability in acute myocardial infarction.

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# 0347

## Beneficial cardiovascular effects of O-GlcNAc stimulation in early phase of septic shock

Marine Ferron* (1), Julien Cadiet (1), Valentine Prat (1), Angélique Erraud (1), Amandine Grabherr (1), Virginie Aillerie (1), Mathieu Mevel (2), John Chatham (3), Bertrand Rozec (4), Chantal Gauthier (4), Benjamin Lauzier (4)
*(1) CHU Nantes, L'Institut du Thorax, Nantes, France – (2) Atlantic Gene Therapies, Nantes, France – (3) Molecular and Cellular Pathology, Birmingham, Grande-Bretagne – (4) CHU Nantes, Hôpital Laennec, Anesthésiologie, Nantes, France*
*Corresponding author: marine.ferron@univ-nantes.fr (Marine Ferron)

*Background* O-GlcNAcylation, a post-translational modification, is the end product of the hexosamine biosynthetic pathway (HBP). Recent studies showed beneficial effects of its increase in acute pathologies, such as hemorrhagic shock. We postulated that increase in total protein OGlcNAcylation at the early phase of septic shock, a systemic inflammation associated with a cardiovascular dysfunction, could improve cardiovascular function and reduce mortality.

*Methods* To induce an endotoxemic shock, rats (n=6-8) received iv either lipopolysaccharide (LPS, 5mg/kg) or saline (CTRL). After 1 h, fluid resuscitation (FR,15mL/kg of colloid, iv) was associated or not with HBP substrate: glucosamine (GlcN, 180mg/kg) or an O-GlcNAcase inhibitor (NButGT, 10mg/kg). Two hours later, echography and mean arterial pressure (MAP) evaluation were performed; blood samples and heart were then collected to evaluate biological parameters (lactate, troponin T) and total O-GlcNAcylation by western-blot.

*Results* In vivo studies showed an hypotension in LPS restored by FR and treatments (MAP: CTRL 87±1, LPS 73±5*, LPS-FR 93±6#, NButGT 83±5, GlcN 92±4mmHg, *: p<0.01 vs CTRL, #: p<0.01 vs LPS) and a systolic dysfunction in LPS with a trend toward an improvement by NButGT and GlcN (ejection fraction: CTRL 80±3, LPS 66±3*, LPS-FR 69±2, NButGT 74±2, GlcN 75±2%, *: p<0.01 vs CTRL). NButGT and GlcN efficiently increased total O-GlcNAc (200 and 300% respectively vs LPS-FR). This effect was associated with a reduced cardiomyocyte insult and tissue dysoxia.

*Conclusions* At the early phase of septic shock NButGT and GlcN induce an increase in cardiac O-GlcNAcylation leading to improve tissue oxygenation and to reduce cardiac injury. These treatments trend to increase the cardiovascular function. Yet, coming studies will evaluate the effect of NButGT and GlcN on mortality.

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